The FDA Sunscreen Study: Lessons Learned and to be Learned

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Overview

- Primary Objective
- Study Design
- Outcomes
- Results
- Lessons learned
- To be learned

Background

- Sunscreens prevent sunburn - reflect or absorb ultraviolet radiation
- Active ingredients are organic chemicals and some have been shown to be absorbed through human skin with detectable levels in the blood or urine
- Sunscreen guidance: Nonprescription Sunscreen Drug Products - Safety and Effectiveness Data
- The guidance requests the assessment of the human systemic absorption of sunscreen ingredients with a Maximal Usage Trial (MUsT)
- This study is not intended to meet all requirements of MUsT studies, but will follow many of the principles to assess maximal use of a single sunscreen formulation

Primary Objective

- To explore whether the active components of 4 sunscreen products are absorbed into the systemic circulation when a sunscreen product is applied under maximal-use conditions
    - Avobenzone
    - Oxybenzone
    - Octocrylene
    - Ecamsule

Tested Products

Avobenzone 3%
Oxybenzone 6%
Octocrylene 2.35%
Homosalate 15%
Octisalate 5%

Avobenzone 3%
Oxybenzone 5%
Octocrylene 10%

Avobenzone 3%
Oxybenzone 4%
Octocrylene 6%

Avobenzone 3%
Octocrylene 10%
Ecamsule 2%

Study Design

- Subjects: Healthy Volunteers; 18 – 60 years
- Open-label, randomized 4 group parallel study

Dose: 2 mg/cm^2
75% of body

Duration: Every two hours, 4 doses/day; 4 days

PK sample: 30 samples
pre-dose to 144 h
(intensive on days 1 & 4)

Outcomes

- **Primary Outcome:**
  - Maximum plasma concentration (Cmax: Day 1 to 7) of Avobenzone
- **Secondary Outcome:**
  - Maximum plasma concentration of Oxybenzone, Octocrylene and Ecamsule
- **Exploratory Outcomes:**
  - C_{max} on day 1 and 4
  - Time at which Cmax occurs on day 1, 4 and overall
  - AUC on day 1, 4 and overall
  - Residual concentrations on each day
  - Half-life of each ingredient
- **Post-hoc Assessments:**
  - Number and percentage of participants with plasma concentration exceeding 0.5 ng/mL on day 1
  - Drug accumulation from day 1 to 4

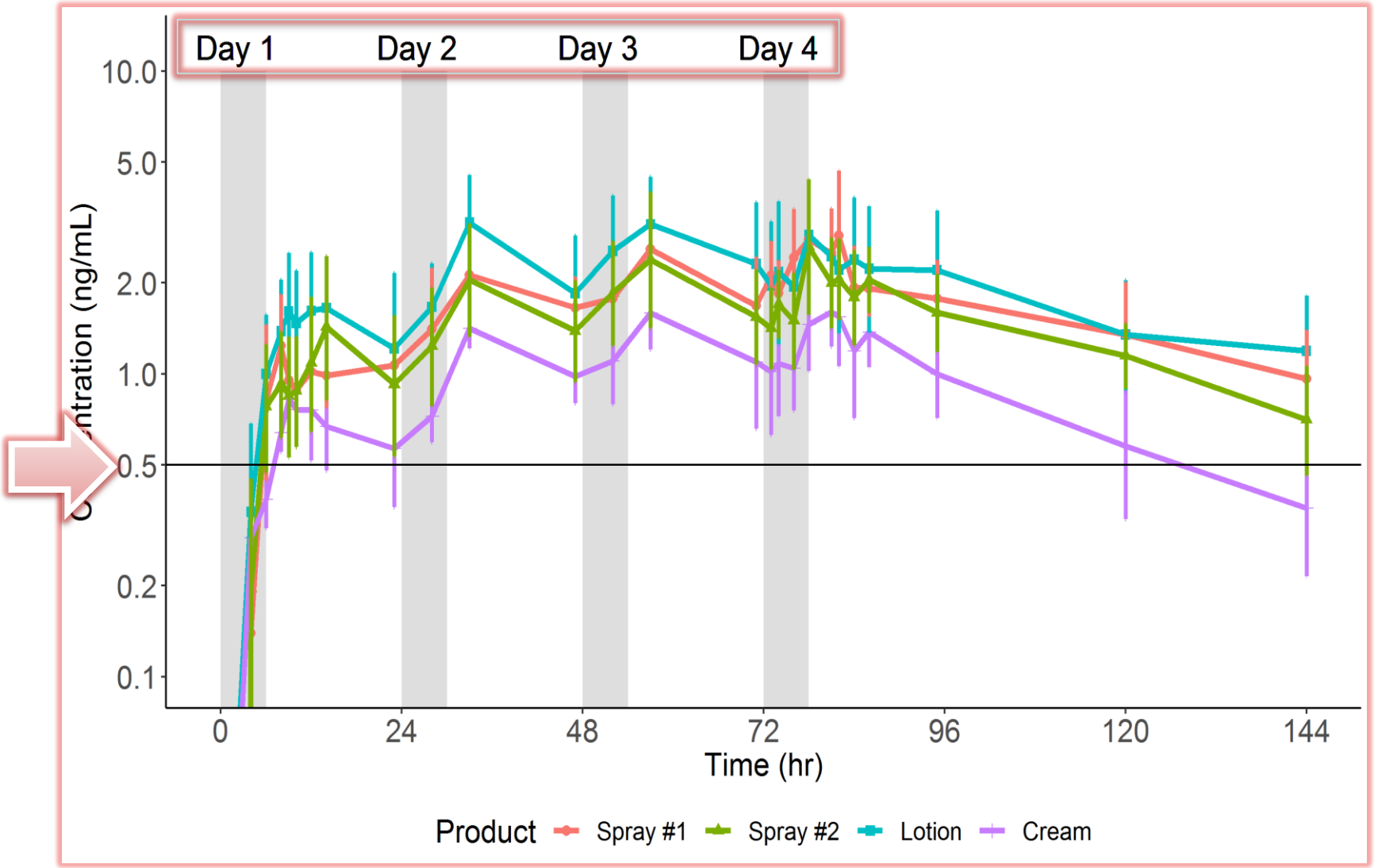
Statistical Analysis

- 24 participants were randomized to receive 1 of the 4 treatments
- Randomization was conducted in block sizes of 4
- Not blinded due to differences in formulation types
- Data was reported with standard descriptive statistics
- Accumulation with repeat dosing was assessed by log-transforming AUC and maximum plasma concentration from day 1 and 4 for each ingredient

Demographics

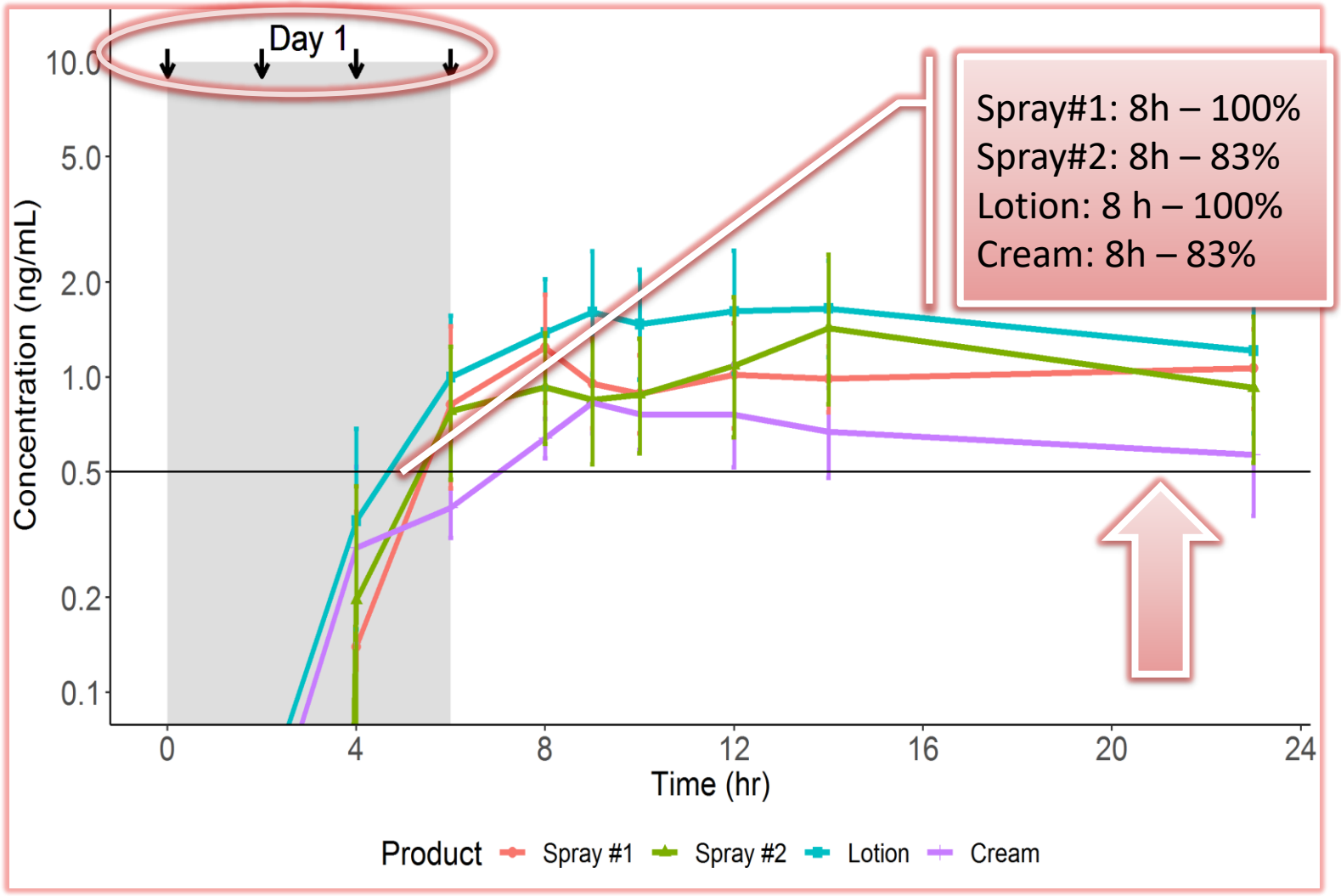
Demographics		Study (N=24)
Age, years (Mean ± SD)		35.5 ± 10.5
Race	Black or African American	14 (58.3 %)
	White	9 (37.5 %)
	Asian	1 (4.2%)
Body mass index, kg/m2 (Mean ± SD)		25.0 ± 2.9
Body surface area, m2 (Mean ± SD)		1.8 ± 0.2
Fitzpatrick skin type	Type 1	0 (0.0 %)
	Type 2	1 (4.2%)
	Type 3	5 (20.8%)
	Type 4	4 (16.7%)
	Type 5	8 (33.3%)
	Type 6	6 (25.0%)

Systemic Exposure of Avobenzone



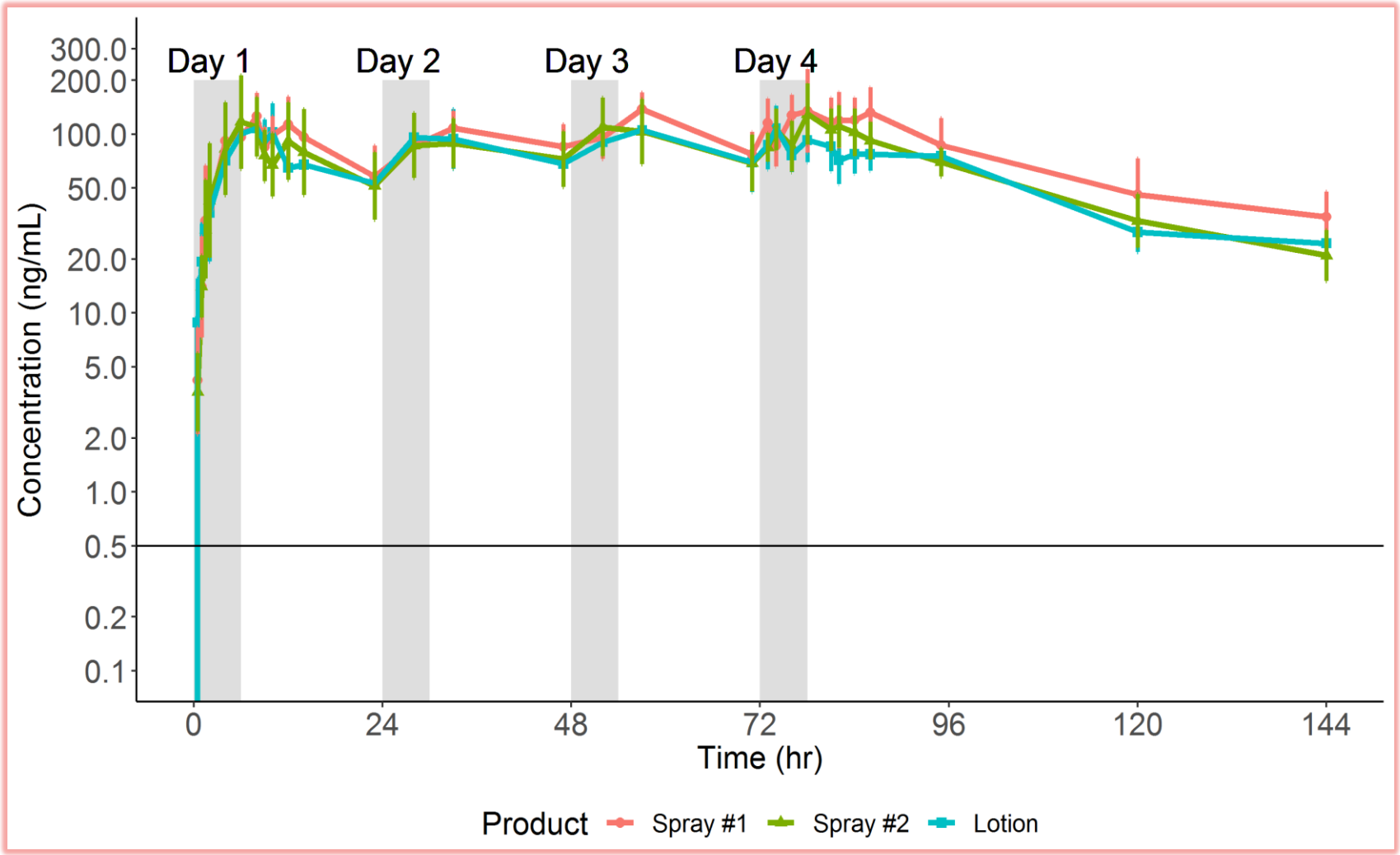
Matta *et al.*, JAMA 2019;321(21):2082-2091

Systemic Exposure on Day 1



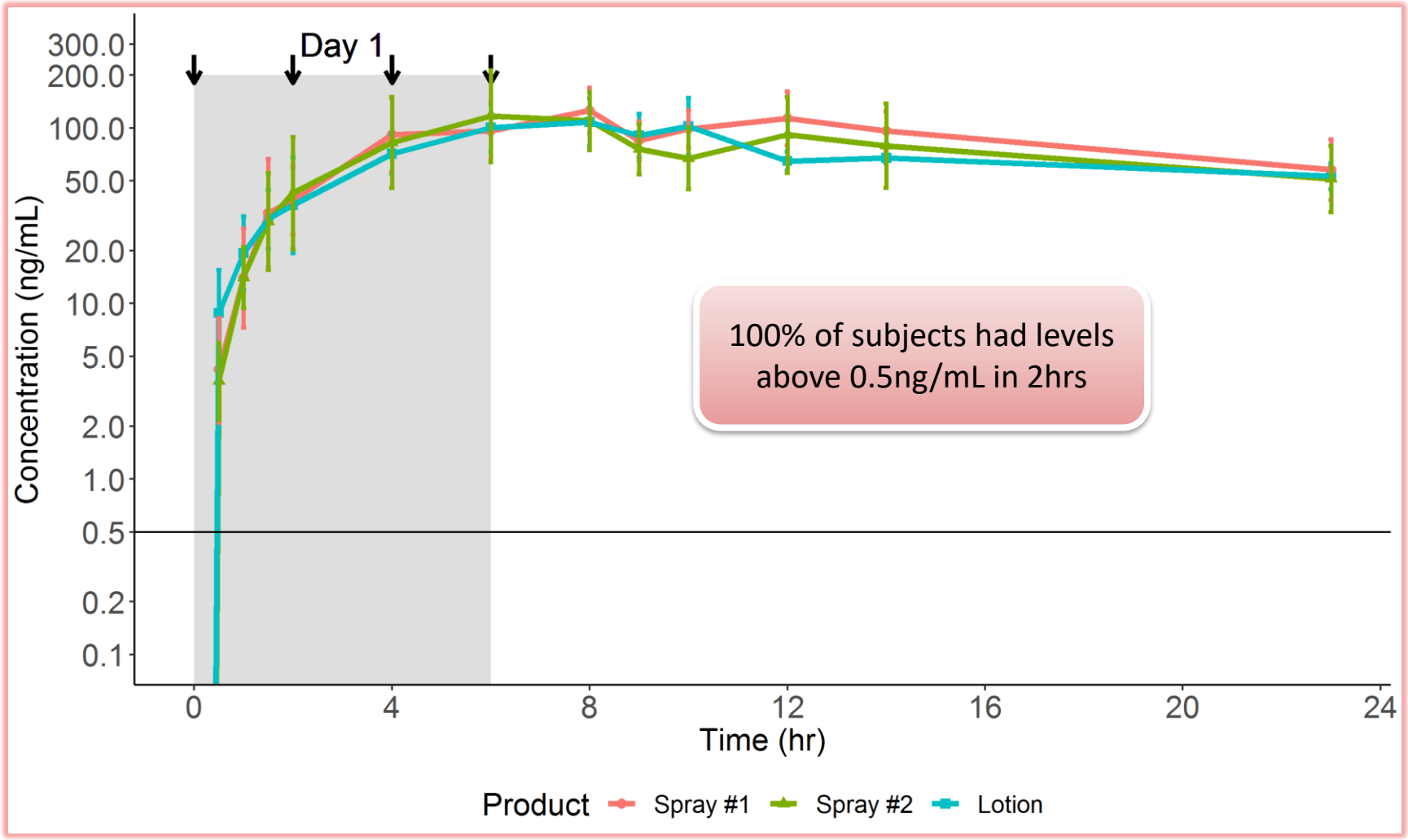
Matta *et al*., JAMA 2019;321(21):2082-2091

Systemic Exposure of Oxybenzone



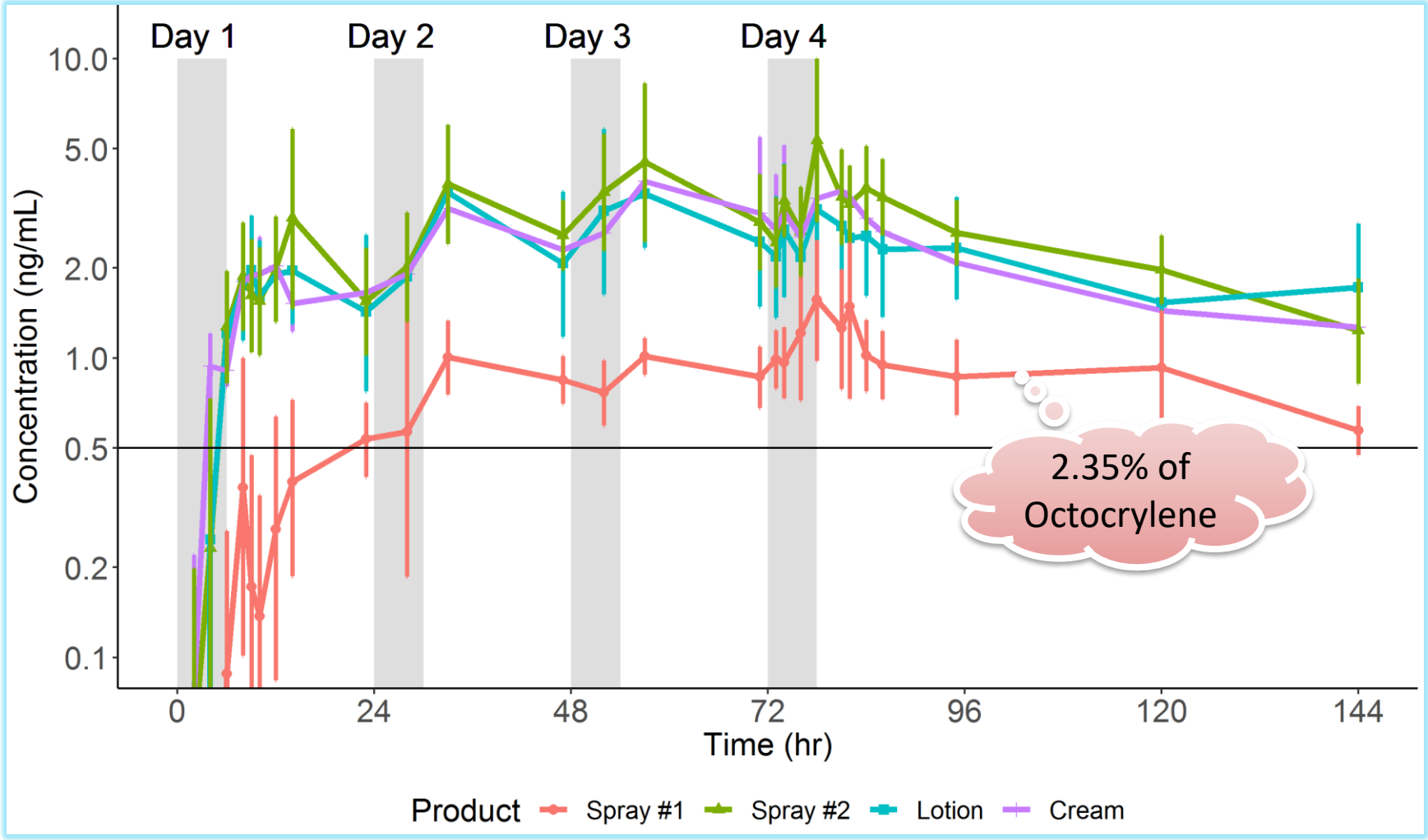
Matta *et al.*, JAMA 2019;321(21):2082-2091

Systemic Exposure on Day 1



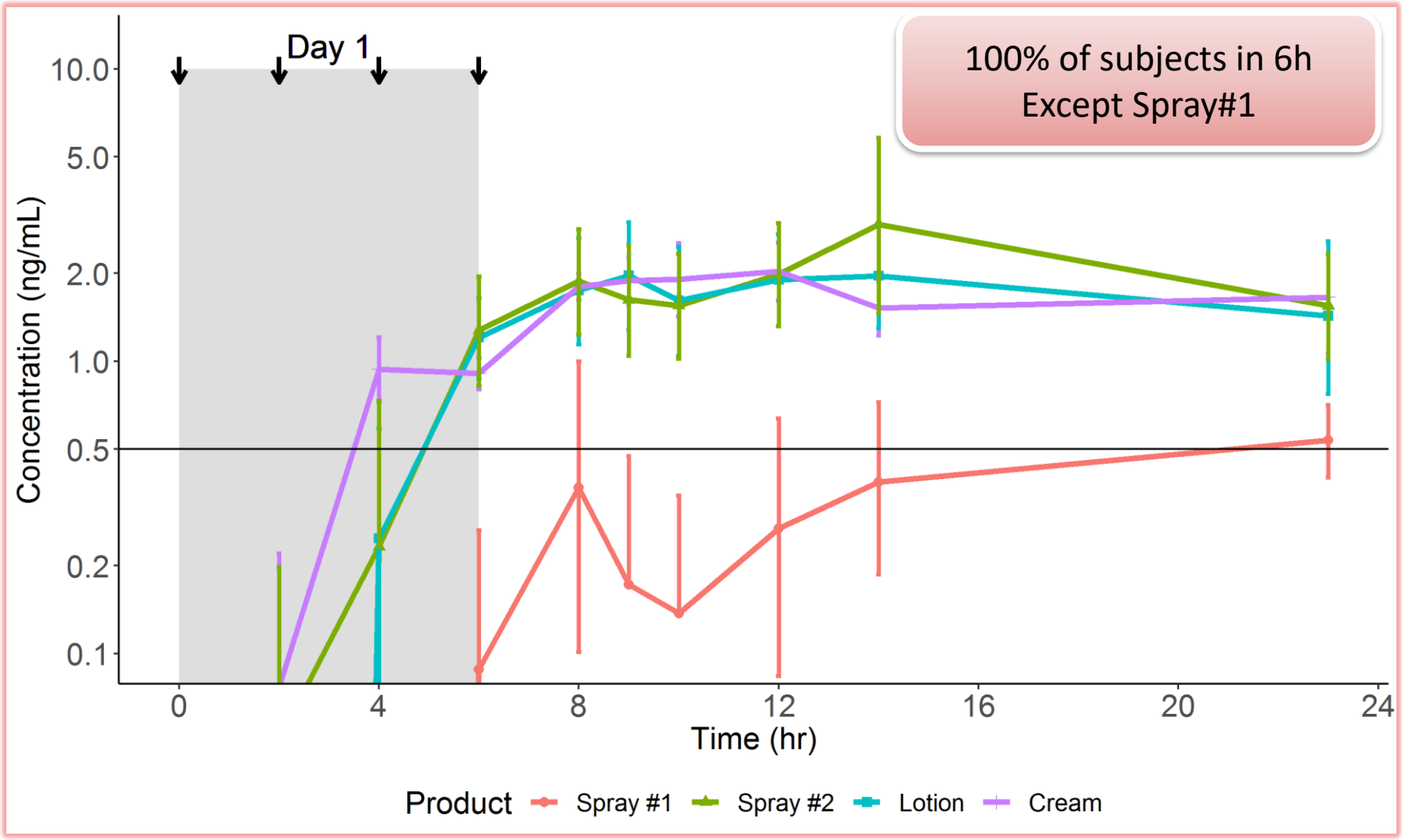
Matta *et al.*, JAMA 2019;321(21):2082-2091

Systemic Exposure of Octocrylene



Matta *et al.*, JAMA 2019;321(21):2082-2091

Systemic Exposure on Day 1



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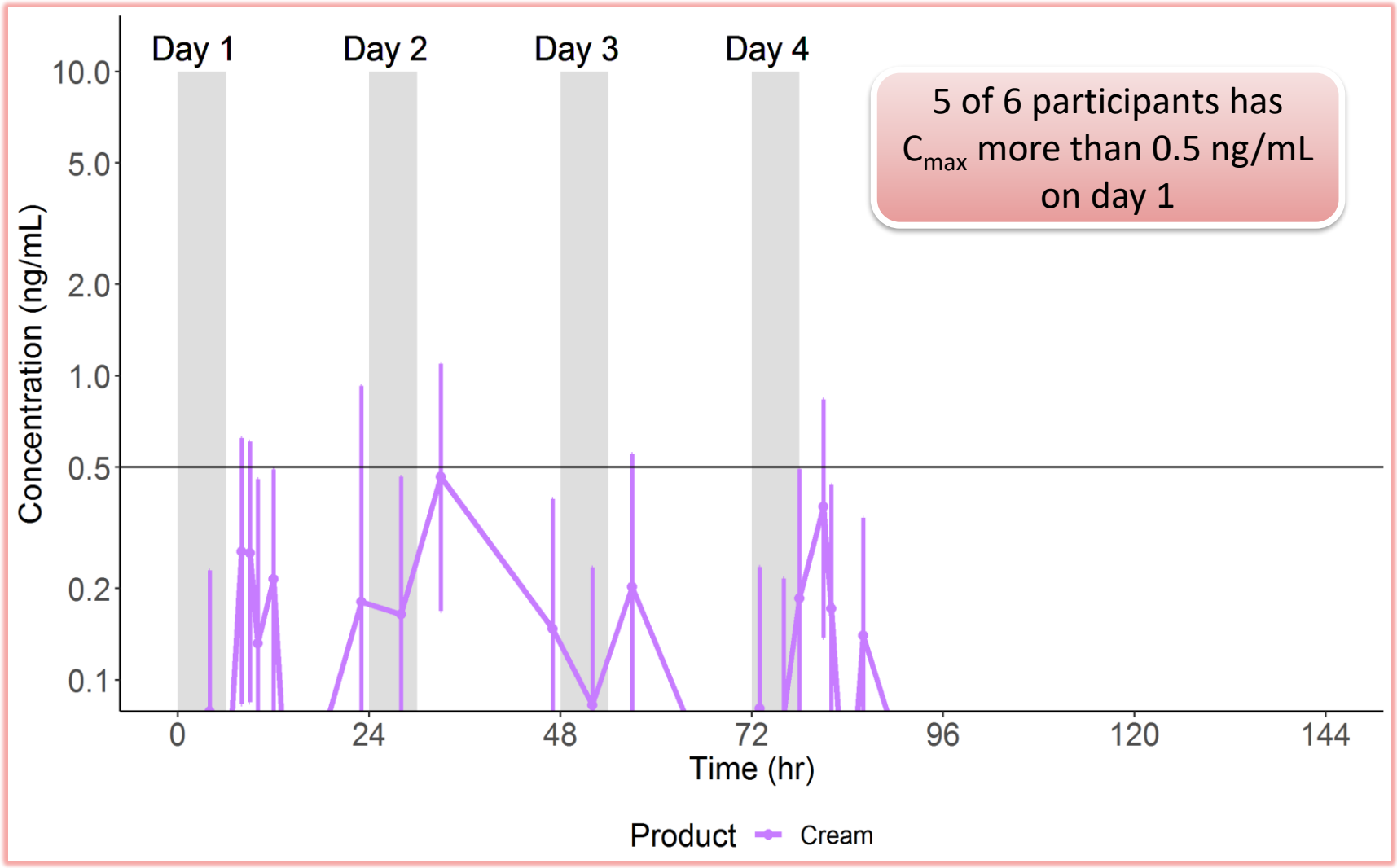
Systemic Exposure of Ecamsule



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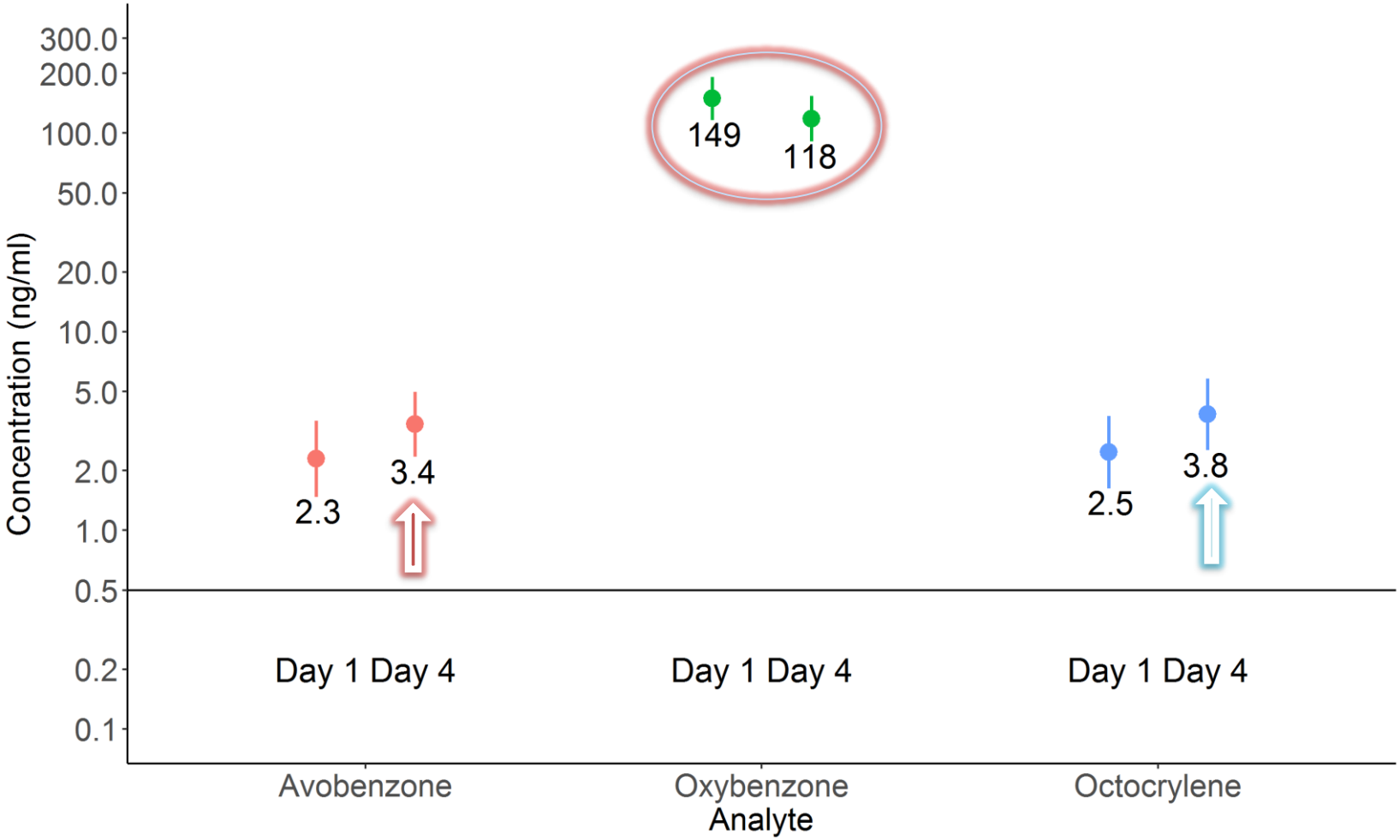
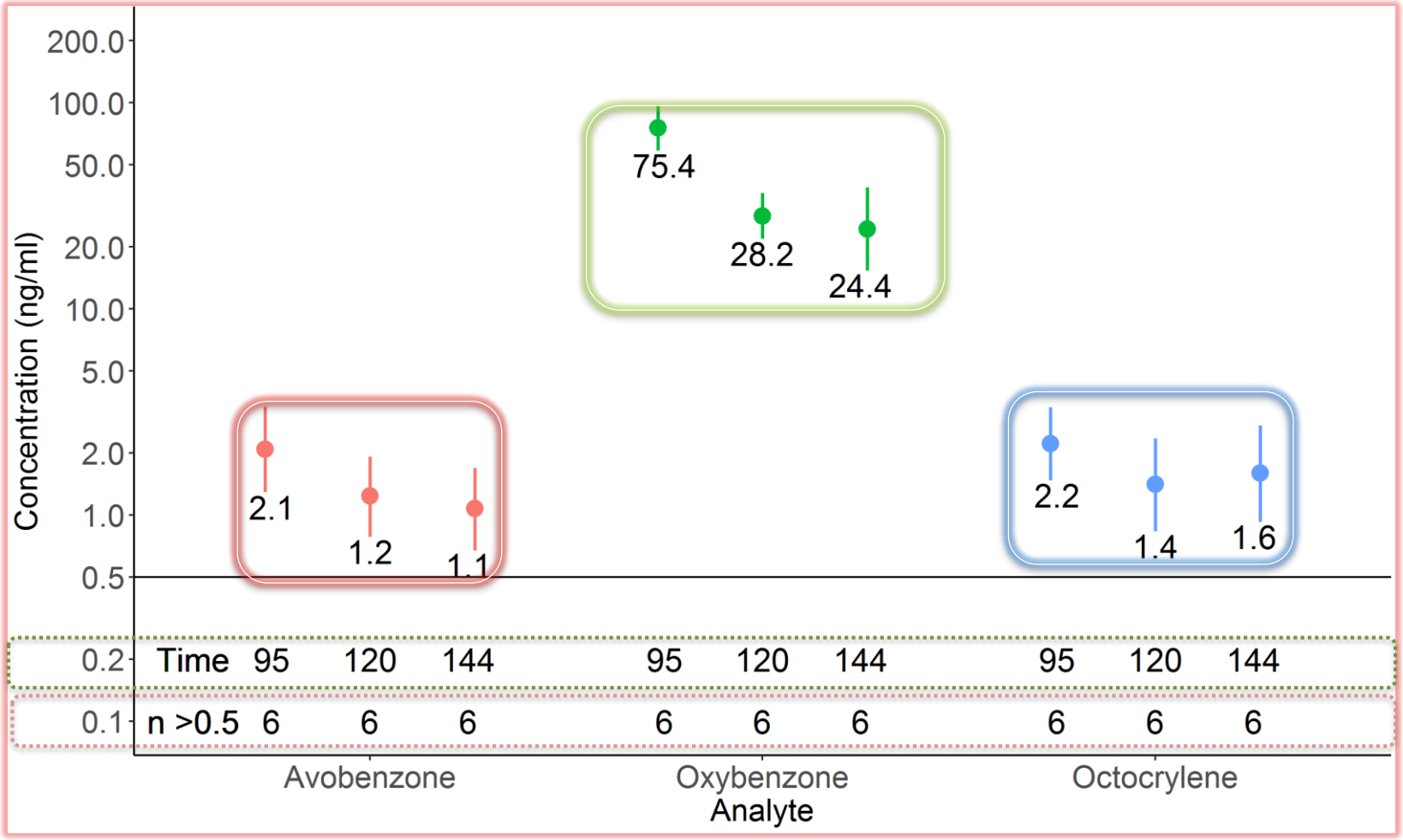
C_{max} on Day 1 versus Day 4



Residual Concentrations



Lessons Learned

- Systemic exposure data of most commonly used ingredients under maximal usage conditions
- 6 subjects is adequate to detect systemic exposure, but was insufficient to quantify any age related changes in absorption due to the small numbers
- All the tested active ingredients in all tested products reached systemic exposures above 0.5 ng/mL
  - All active ingredients reached above 0.5 ng/mL on day 1
- All tested ingredients have long terminal half-lifes
  - Could be skin is serving as a depot

To be learned

- Systemic exposure after a single application
- Time to clear from body
- Metabolites and their systemic exposures
- Toxicity of these active ingredients
- Systemic exposure in pediatrics
- Role of covariates such as age across the population

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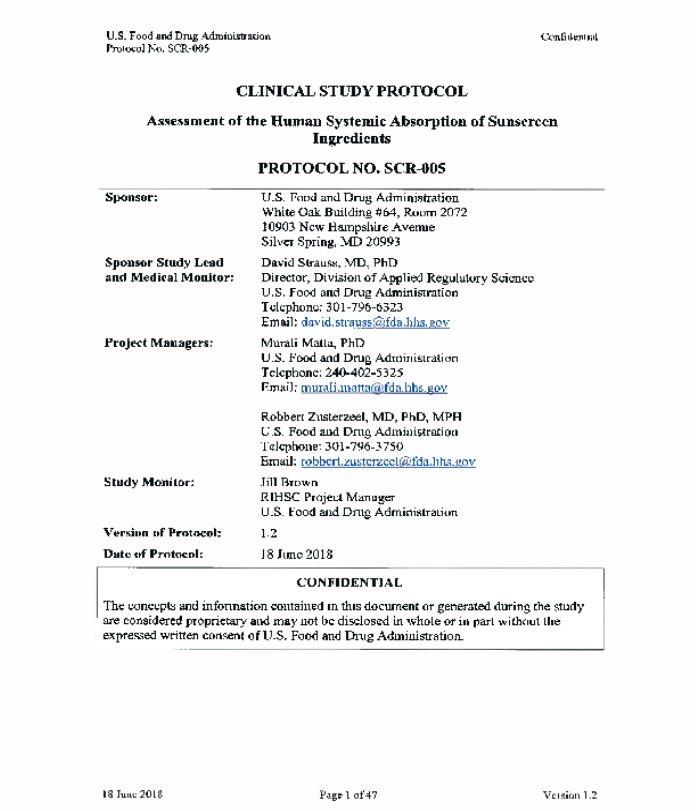
THANK YOU
SUN
SCREEN
SPF 50

Back Up

- Clinical Protocol



U.S. Food and Drug Administration
Protocol No. SCR-005

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CLINICAL STUDY PROTOCOL

Assessment of the Human Systemic Absorption of Sunscreen Ingredients

PROTOCOL NO. SCR-005

Sponsor:	U.S. Food and Drug Administration White Oak Building #64, Room 2072 10903 New Hampshire Avenue Silver Spring, MD 20993
Sponsor Study Lead and Medical Monitor:	David Strauss, MD, PhD Director, Division of Applied Regulatory Science U.S. Food and Drug Administration Telephone: 301-796-6323 Email: david.strauss@fda.hhs.gov
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Study Monitor:	Jill Brown RIHSC Project Manager U.S. Food and Drug Administration
Version of Protocol:	1.2
Date of Protocol:	18 June 2018

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Statistical Analysis Plan

SCR-005: Assessment of the Human Systemic Absorption of Sunscreen Ingredients

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Study Monitor:	Jill Brown RIHSC Project Manager U.S. Food and Drug Administration
Version of SAP:	1.1
Date of SAP:	16 July 2018

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Consort Diagram